

WHO Information Notice for IVD Users

Nucleic acid testing (NAT) technologies that use real-time polymerase chain reaction (RT-PCR) for detection of SARS-CoV-2

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Español

Product type: Nucleic acid testing (NAT) technologies that use real-time polymerase chain reaction (RT-PCR) for detection of SARS-CoV-2

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Purpose of this notice: To ensure users of certain nucleic acid testing (NAT) technologies are aware of certain aspects of the instructions for use (IFU) for all products.

Description of the problem: WHO has received user feedback on an elevated risk for false SARS-CoV-2 results when testing specimens using RT-PCR reagents on open systems.

As with any diagnostic procedure, the positive and negative predictive values for the product in a given testing population are important to note. As the positivity rate for SARS-CoV-2 decreases, the positive predictive value also decreases. This means that the probability that a person who has a positive result (SARS-CoV-2 detected) is truly infected with SARS-CoV-2 decreases as positivity rate decreases, irrespective of the assay specificity. Therefore, healthcare providers are encouraged to take into consideration testing results along with clinical signs and symptoms,

confirmed status of any contacts, etc.

Users of RT-PCR reagents should read the IFU carefully to determine if manual adjustment of the PCR positivity threshold is necessary to account for any background noise which may lead to a specimen with a high cycle threshold (Ct) value result being interpreted as a positive result. The design principle of RT-PCR means that for patients with high levels of circulating virus (viral load), relatively few cycles will be needed to detect virus and so the Ct value will be low. Conversely, when specimens return a high Ct value, it means that many cycles were required to detect virus. In some circumstances, the distinction between background noise and actual presence of the target virus is difficult to ascertain. Thus, the IFU will state how to interpret specimens at or near the limit for PCR positivity. In some cases, the IFU will state that the cut-off should be manually adjusted to ensure that specimens with high Ct values are not incorrectly assigned SARS-CoV-2 detected due to background noise.

Manufacturers regularly review the design of their product, including labelling and IFU based on customer feedback. In the early phases of the COVID-19 pandemic, in vitro diagnostics (IVDs) were rapidly developed, validated and verified, and then rolled out. Therefore, it is not unexpected that IVDs may require refinement based on user feedback after their introduction at scale. Users should verify the version of the IFU with each consignment they receive to see if any changes have been made to the IFU.

Advice on action to be taken by users:

1. **Please read carefully the IFU in its entirety.**
2. **Contact your local representative if there is any aspect of the IFU that is unclear to you.**
3. **Check the IFU for each incoming consignment to detect any changes to the IFU.**
4. **Consider any positive result (SARS-CoV-2 detected) or negative results (SARS-CoV-2 not detected) in combination with specimen type, clinical observations, patient history, and epidemiological information.**
5. **Provide the Ct value in the report to the requesting healthcare provider.**

Transmission of this WHO Information Notice for Users:

Please disseminate this notice to all those who need to be aware within your organization or to any organization where the potentially affected product has been deployed and used.

Contact person for further information:

Anita SANDS, Regulation and Prequalification, World Health Organization, e-mail: sandsa@who.int

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